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THE PRESIDENT'S ADDRESS.

SOME CONSIDERATIONS ON THE PHENOMENA OF PARASITISM AMONGST PROTOZOA.

By Prof. E. A. Minchin, M.A., F.Z.S.

(*Delivered February 22nd*, 1910.)

A living organism, whether plant or animal, which gains its livelihood at the expense of another organism is termed a parasite, and the organism at whose expense it lives is termed its host. The conception of parasitism, therefore, implies an antagonistic relationship between two correlated beings, parasite and host, each of which has, so to speak, its own point of view, the one attacking, the other defending. The phenomena of parasitism are of most wide-spread occurrence, and very varied in their nature. There is probably no species of non-parasitic organism which is not liable to the attacks of some parasite, and the same holds true even of a great number of parasites themselves, which are subject to be attacked in their turn by some other parasite.

The problems of parasitism are very complex, and are also very important, both from the more abstract point of view, as problems of natural history and bionomics, and also from the practical point of view, in their bearing upon questions of medical and veterinary science. In a brief space it is not possible to discuss all aspects and problems of parasitism, nor can such a discussion lay claim to any finality in the present

state of our knowledge. I propose to lay before you a few facts of parasitism, restricting myself entirely to the field of the Protozoa, and to consider the phenomena solely from the point of view of natural history; a method of treatment which, though it cannot claim to solve all difficulties, may serve nevertheless to furnish certain guiding principles, and to throw some light, if only a side-light, on the questions at issue.

Amongst Protozoa, as is well known, many different modes of life occur. We are concerned here with those species which live constantly in association with some other organism of a distinct kind. Such a species may live either upon, or in, the organism with which it is associated; in the first case it is then termed *epizoic*, in the second *entozoic*. In all such cases of association, the species which are truly parasitic must be clearly distinguished from those which are not. Taking first the case of epizoic forms, it is found that in many cases they merely utilise the body of their host as a coign of vantage where they readily obtain their food, or as a convenient means of transport, especially when the epizoic form in question is of a sessile habit of life. Every naturalist is acquainted with the sea-anemones that live upon hermit-crabs, to the advantage probably of both animals, at all events to the detriment of neither. There are many similar cases amongst the Protozoa. As every microscopist knows, the appendages of many Crustacea, especially of Cladocera, such as *Daphnia*, and Copepoda, such as *Cyclops*, are often thickly beset with sessile Vorticellids or Acinetans, which obtain a convenient lodging but provide their own board. Other forms occur on the stems of Hydroids, as for example *Acineta papillifera* on *Cordylophora lacustris* (Hickling Broad, Norfolk). The common *Hydra* often bears a beautiful Infusorian which from its louse-like appearance has the name *Trichodina pediculus*, but which caters for itself and not at the expense of the *Hydra*. Amoebae are to be found creeping on the exterior of calcareous sponges, nourishing themselves on diatoms and other organisms. Similar instances could be multiplied indefinitely of epizoic species which are merely commensals, and not parasites in any sense of the word.

On the other hand, epizoic forms may be parasites, and even dangerous parasites, nourishing themselves at the expense of the animal they infest, and sometimes inflicting much damage upon it. It can easily be understood that an epizoic form which at first lived harmlessly upon some animal, drawing its supplies of food from the surrounding medium, might acquire the habit ultimately of obtaining its nourishment from the living substratum upon which it has planted itself. Examples of truly parasitic epizoic forms are the Flagellate *Costia necatrix* and the Infusorian *Ichthyophthirius*, both of which live on the skin of fishes and injure the epidermis.

In like manner, there are many entozoic Protozoa which inhabit the bodies, and more especially the intestines, of other animals, but which are not to be considered as true parasites; they simply feed on various substances to be found there, such as waste particles of food or faecal matter, or on other organisms, such as Bacteria—in short, on material which, from the point of view of the host, is superfluous or even noxious. Thus entozoic Protozoa may be quite harmless, perhaps even useful as scavengers to their host; but such forms may also readily acquire truly parasitic habits and become a danger to their hosts. A good example of this is seen in the amoebae found in the intestine of man. One species, *Amoeba coli*, which occurs commonly in man in all countries, is believed to be a harmless entozoic form. In the tropics, however, other species occur which find a more abundant source of nutrition in the living body which harbours them; they attack the epithelium and tissues of the intestine, devouring cells and blood-corpuscles and giving rise to a virulent form of dysentery; and they penetrate into the liver, where they destroy and corrode the tissues, producing most dangerous abscesses. It is often very difficult to draw the line between harmless and harmful entozoic Protozoa, but all such organisms must be considered suspect, and it is the safest course from the practical point of view to hold them guilty until they have been proved innocent.

The entozoic Protozoa which are truly parasitic are found inhabiting a variety of situations in the bodies of their hosts. In

some cases the host is another species of Protozoon, into the body of which the intruder penetrates, living either in its cytoplasm or its nucleus. Amoebae are very subject to the attacks of intra-nuclear parasites, and the young stages of many Acinetans are parasitic upon other Infusoria. When the host is one of the Metazoa, the invading organism may be, in like manner, intra-cellular or intra-nuclear in habitat; or it may penetrate into the tissues, living amongst and between the constituent cells; or, finally, it may be found in one of the internal cavities of the body, such as the digestive tract, body-cavity, blood or lymph-spaces, urinary organs, etc., either living free in the cavity or attached to the lining epithelium. We may distinguish, in general, two ways in which these parasites may tax the resources of the host. Some of those living in the digestive tract may simply absorb the soluble products of digestion occurring there, thus diminishing the nutriment of the host by intercepting its food-supply. Other parasites, in the digestive tract or elsewhere, ravage the very substance of the body of the host, either by devouring cells and tissues, as in the case of the dysenteric amoebae already mentioned; or, and more usually, by absorbing the vital fluids and juices of the cells, tissues, or organs into which they penetrate, sapping in many cases the life-springs of the organism that harbours them.

As diverse as the modes of parasitism amongst Protozoa are the effects they produce upon their hosts. Some forms of these parasites cause no perceptible disturbance in the well-being of the host; even when they destroy cells and portions of the tissues, the damage may be slight, and is quickly made good without appreciable harm being done to the host. From this condition of more or less perfect harmlessness there is a continuous gradation in the ascending scale of capacity for harmfulness possessed by Protozoan parasites, culminating in species which bring about the death of their hosts with greater or less rapidity. Hence, parasitic Protozoa are commonly characterised as pathogenic, that is to say disease-producing, and non-pathogenic; these two terms imply, however, a distinction which is purely relative, since a "disease" may be anything from a slight and transitory

indisposition to a severe and fatal illness. Hence, in discussing these parasites it is better to group them as lethal, or deadly, and non-lethal, including under the latter term both harmless parasites and those that produce ailments from which the host recovers more or less easily. The distinction between lethal and non-lethal parasites is not, however, in all cases absolute, since a parasite which is ordinarily harmless or but slightly harmful may exhibit lethal powers under certain conditions, especially when the host is in an enfeebled state of vitality from other causes. For instance, it is common to see animals living in captivity succumb to the effects of parasites which are harmless to them when living a natural healthy life in their wild state. The weakened powers of resistance of the host enable the parasite to flourish in an abnormal manner, and give it a capacity for harmfulness which it does not possess naturally. Hard and fast distinctions between different classes of parasites, from the point of view of the effects on their hosts, cannot always be drawn.

The great diversity in the effects of Protozoan parasites is very remarkable, and furnishes a most important subject for consideration and investigation. It would seem, at first sight, as if the presence of even a single parasite must cause some bad effect in the body of the host, even if the disturbance be so slight as to produce no appreciable symptoms of ill-health in the organism as a whole. If so, then the greater the number of parasites in the body of the host, or the larger the parasite itself, the greater should be the derangement in the health of the host. Consequently, the greater the powers of multiplication within the body of the host possessed by any given parasite, the more dangerous it might be expected to be. To a certain extent this expectation is realised. Thus the Gregarines of the suborder Eugregarinae, found commonly in the bodies of insects and other arthropods, are amongst the most harmless of parasites, so far as can be judged, and in these forms endogenous multiplication, as it is called, that is to say multiplication in the actively parasitic phase in the body of the host, does not take place. On the other hand, the parasites of the closely allied order Coccidia

begin their cycle of development in the host by very active endogenous multiplication, overrunning some particular organ or tissue, and producing a sick and enfeebled condition which brings the host often to the verge of death, and sometimes even kills it. As a rule, however, animals attacked by coccidiosis, as the disease is termed, recover from the malady owing to the fact that when the host is brought very low, its condition appears to react on the parasite, with the result that the parasite ceases to multiply endogenously and enters upon a different reproductive phase; it produces resistant stages destined to infest new hosts, in the form of cysts and spores, which are inactive and do not absorb nutriment, but pass out of the body of the host. In consequence the diseased animal loses its parasites, or the greater number of them, and the tissues are left in peace to regenerate and repair their injuries, provided they have not gone beyond the point at which recuperation is possible.

If the action and reaction of host and parasite were relations dependent simply on the number or bulk of parasites present in the body of a given host, the problems of parasitism would be comparatively simple. Examples can be brought forward to show that in many cases the effects produced by Protozoan parasites cannot be explained, either by the number of parasites present or by the aggregate bulk of the parasites in proportion to that of the body of the host. The effect produced by a given species of parasite on a given species of host is a specific reaction, which differs markedly when one of the two factors is varied. It is not uncommon to find insects with their digestive tract or body cavity crammed with parasitic gregarines, of relatively large size, but causing no apparent inconvenience to the host. On the other hand large mammals may be killed by minute organisms in scanty numbers. A better comparison is furnished by considering closely allied parasites and hosts respectively. A rat may have its blood swarming with *Trypanosoma lewisi*, without being apparently any the worse for it. On the other hand, in a man dying of sleeping sickness, caused by *T. gambiense*, or in a ruminant dying of nagana (tsetse-fly disease), caused by *T. brucii*, the trypanosomes may be so scanty as to be exceedingly

difficult to detect.* These facts strongly suggest, as has been pointed out by medical authorities, that the parasites produce a specific toxin. Only in a single case, however, has it been claimed that a toxin has been isolated from a Protozoan parasite, namely the "sarcocystine" produced by the parasites of the genus *Sarcocystis* (Sarcosporidia).† The subject is one which remains to be investigated, and in the present state of knowledge it would be unprofitable to discuss it further here.

The interaction of host and parasite is a question of great practical importance, which in consequence has been studied chiefly from the medical standpoint, that is to say, from the point of view of the host. I propose here, as I have already said, to deal with the question as a naturalist, and to discuss the problem rather from the point of view of the parasite; and with this object I shall begin by a brief consideration of the facts of parasitism in general.

A parasite is, like any other living being, an organism struggling for existence in a hard and cruel world. The difficulties, however, against which a parasite has to contend, in the struggle for existence, are different in many respects from those which beset a free-living organism. When once a parasite has obtained a footing in its proper host, the question of food-supply is solved for it, since it finds itself lodged in the midst of abundant nutrition so long as its host lives. On the other hand, if the species is to be maintained, it is essential that the offspring of the parasite should be able to infect new hosts—a matter usually of great difficulty, and one in which the chances are all against the parasite in most cases. To ensure dissemination of the species a large number of offspring must be produced, and special adaptations and mechanisms may be necessary. Hence in parasites, the more they become specialised and adapted to parasitic life, the more the organs and functions of nutrition tend to become simplified, and the greater the tendency to elaboration of the reproductive system. It is especially amongst parasites

* Compare Laveran and Mesnil, "Trypanosomes and Trypanosomiases," translated by Nabarro (Baillière, Tindal & Cox, 1907), pp. 146–150.

† *Comptes Rendus Soc. Biol. Paris* LI. (1899), pp. 311–14.

that we find the greatest complication in the structure and mechanisms of the generative organs, the most extraordinary and delicately-adjusted adaptations of the propagative phases, and the most astonishing fertility.

So long as the parasite has not made the necessary provision for propagating its kind and disseminating its progeny, it is against its best interests to kill or greatly weaken its host. The interests of the two are bound up together, and the death of the host, before the parasite has completed its reproductive arrangements, necessarily entails the extinction of the parasite. The ideal host, from the point of view of the parasite, is one that is "tolerant," that is to say, one that can support the presence of the parasite and keep it supplied with the nutriment it requires, like a good mother or nurse, without suffering in health and vigour to any marked extent. When once, however, the parasite has matured and produced its reproductive phases, the life or death of the host may be a matter of indifference to it. In some cases the death of the host may even be necessary for the dissemination of the parasite.

From these general considerations it is seen that reproduction, and above all the dissemination of the progeny in a manner adapted to the special circumstances of its mode of life, are by far the most important functions of a parasite. Turning now to the special consideration of Protozoan parasites, we find that diverse conditions of their mode of life and habitat impose a corresponding diversity in their reproductive phases and their modes of dissemination.

The passage of a parasite from one host to another includes two manœuvres, so to speak: the passing out from the first host, and the passing into the second. Primitively it may be supposed that this migration was effected simply by the unaided efforts of the parasite itself, that is to say, that the active motile parasite would force its way out of one host, move freely in the surrounding medium, and sooner or later attack and penetrate a second host. This primitive method of transference doubtless occurs in many cases, especially amongst epizoic forms. In the case of entozoic forms its occurrence is more doubtful. It is

very probable, however, that the spirochaetes found infesting certain bivalve molluscs, such as *Spirochaeta balbianii* of the oyster, and *S. anodontae* of the pond-mussel, swim out of one mollusc and into another. Active migration of this kind, however, is very rare amongst entozoic parasites, if it occurs at all. In the first place the conditions of life within a living body, in the midst of organic fluids, are so different from those in the open water, whether salt or fresh, that it is hardly to be expected that a delicate unicellular organism adapted to the one mode of life could stand the sudden change to the other. In the second place, it is clear that active migration of parasitic Protozoa could only be effected when the host is an aquatic animal, and not when it is a terrestrial organism. The only instances of active migration of entozoic parasites known with certainty are those in which the parasite can penetrate a mucous membrane, and is thus able to pass from one host to another when two such surfaces are in contact. In this way the trypanosome of dourine in horses (*T. equiperdum*) passes from one host to another during coitus, and the transmission of the parasite of syphilis is another instance.

Speaking generally, and excluding for the moment those cases in which the transmission is brought about by means of an intermediary host, the propagative phases of Protozoan parasites take the form of inactive, resting stages in which the body of the parasite is protected against adverse external conditions by a tough protective membrane. In the form of resistant cysts or spores the parasites in a dormant state brave the rigours of the external world, and are able to withstand the heat and drought of summer, the cold and frost of winter. Like seeds they offer an inert resistance to the elements and are disseminated passively, and like seeds they germinate when they reach a suitable soil, but not till then.

Let us consider now the manner in which the first step in the propagation is effected, that is to say, how the propagative phases leave the body of the host.

Many, perhaps the majority of Protozoan parasites occupy positions in the body of the host whence the propagative phases can pass without difficulty to the exterior. This is the case when

the parasite is lodged in organs which have ducts or passages opening directly or indirectly to the exterior: for instance, in the digestive tract and its dependences, such as the liver, salivary glands, malpighian tubules of insects, etc.; or the urinary organs and ducts. In all such cases the propagative phases of the parasite pass harmlessly to the exterior. The host may in this manner get rid entirely of its parasites, without however necessarily acquiring immunity to fresh infections; or, on the other hand, the parasite may keep up its numbers in the host by "endogenous" multiplication while at the same time it is continually sending forth the propagative phases destined to infect new hosts. In the majority of Protozoan parasites the relations to the host are of this type, and the parasites are neither lethal nor pathogenic to any great extent.

On the other hand, there are many instances in which Protozoan parasites occupy a position in the body of the host whence escape by anatomical channels is not possible, or if possible, not suitable. This is the case when the parasite inhabits some enclosed space in the body, such as the coelome or general body-cavity, or the blood-system; or when it attacks deeply-seated cells or tissues of the body. In such cases there are at least six known methods whereby the parasite is disseminated or transferred to fresh hosts.

1. The resistant stages of the parasite may be set free by the death and decay of its host. This appears to be the manner in which some of the tissue-infecting parasites of the order Myxosporidia, especially the family *Myxobolidae*, are disseminated. These organisms are for the most part parasites of fishes, and are often very deadly in their effects.

2. The parasite may cause tumours and ulcers, which suppurate and so set free the spores or cysts of the parasite. This again is an effect commonly produced by tissue-parasites such as the *Myxobolidae*. In such cases the parasite is always pathogenic and frequently lethal to the host.

3. The parasite remains in the host until the latter is eaten by some animal which preys upon it. The propagative phases of the parasite are able, however, to resist digestion by the

animal that has devoured their former host, and pass unaltered through its intestine, to be finally cast out with the dejecta. This is almost certainly the method by which the common *Monocystis* of the earthworm infects its host. The parasite produces resistant spores in the worm; the worm is eaten by a bird, mole, frog, or some other animal, through the digestive tract of which the spores of the *Monocystis* pass unaltered; they are scattered abroad with the faeces, and may then be swallowed by another earthworm, in which they germinate and produce an infection.

4. As in the last case, the host, together with its parasites, is devoured by some animal, in which, however, the parasite is not merely carried passively, but becomes again actively parasitic. Hence in this case there is an alternation of hosts, one of the two hosts becoming infected by devouring the other. This mode of infection, which is well known to be of frequent occurrence amongst certain parasitic worms, such as Cestodes (tapeworms), is probably also frequent amongst Protozoa; but at present only one case of it is known with certainty, that of the species of the genus *Aggregata*, parasites of crabs and of Cephalopods, such as the cuttle fish and the octopus. In the Cephalopod the parasite forms resistant spores which pass out with the faeces and may then be devoured by crabs: in the crab the spores germinate and give rise to a second form of the parasite which lives and multiplies in its new host. If, as frequently happens, the crab is devoured by a cephalopod, the parasite completes its life-cycle by becoming once more a parasite of the cephalopod.

5. The Protozoa parasitic in the blood of vertebrates are disseminated in all cases, apparently, by bloodsucking invertebrates, such as leeches, ticks, or insects, which take up the parasites by sucking the blood of an infected animal. Later on the parasite may be inoculated into a second vertebrate host by the bloodsucking invertebrate when it sucks blood at a later feed. In some cases the transference of the blood-parasite from one vertebrate host to another may be effected in a purely mechanical manner by the invertebrate, but in most cases the invertebrate is a true host in which the parasite multiplies and goes through a cycle of development. Hence in such cases also there is an

alternation of hosts and a complicated life-cycle, which has been most completely studied in the case of the malarial parasites of man, transmitted by the agency of mosquitoes.

6. In some cases the parasite may penetrate the ovary of its host, pass into the ova, and thus infect the embryo and the next generation of the host. Transmission of this kind is known in a certain number of cases: for instance, in the "pébrine" disease of silkworms caused by *Nosema bombycis*. It is never the sole method of transmission, but is always supplementary to other methods.

To turn now to the methods by which Protozoan parasites penetrate into new hosts. We find four known methods, which can be summarised very briefly after what has been stated already. The commonest is the method of casual or contaminative infection, where the host infects itself by taking up the propagative phases of the parasite accidentally from its surroundings. Most usually infection takes place by way of the mouth, with the food; but it may be effected by the respiratory organs. Other modes of infection are the contagious, as in dourine already mentioned; the inoculative, as in malaria and other diseases caused by blood-parasites; and the so-called hereditary method, as in *Nosema bombycis* and other cases.

From the foregoing summary of the methods by which Protozoan parasites are propagated and spread from one host to another, it is clearly seen that there are only very few cases in which it is of direct advantage to the parasite to cause the death of the host, and even then only when the propagative phases of the parasite are fully matured. In cases where the parasite is disseminated by its host being devoured by another animal, it is necessary for the propagation of the parasite that the host should die a violent death, but not through the agency of the parasite; on the contrary, the interests of the parasite are best served by the host remaining in good health until the fatal moment arrives, unless it be supposed that some weakening of the host renders it more liable to become the prey of its enemies. Blood-parasites, transmitted by the inoculative method, are not perceptibly benefited by the host's illness, and certainly not by its death. It is, however, very necessary for this method of dissemination that the required

phases of the parasite should be sufficiently abundant in the blood to make sure of infecting the invertebrate that sucks the blood and transmits the parasite. To ensure this taking place it is essential that the parasite should multiply and swarm in the blood to an extent that may, in many cases, lead to pathogenic and even fatal results. Hence one interest of the parasite may, so to speak, clash with another, and the all-important object of dissemination cannot be attained without bringing about a state of affairs which puts an end to the host and to the parasite with it; a result which, though detrimental to the parasite, may not be seriously so, if the death of its host do not supervene until there has been time for the dissemination of the parasite to have taken place. No reasonable person, however, could expect any adaptation to be absolutely perfect.

The inevitable conclusion from a general consideration of the facts of parasitism amongst Protozoa is, therefore, that it is hardly ever to the advantage of the parasite to be pathogenic, and still less so to be lethal to its host. This conclusion is borne out by the facts, for when the known forms of Protozoan parasites are reviewed and considered in their entirety, it is found that the vast majority of them are quite harmless to their hosts. Pathogenic and lethal parasites are the exception amongst the Protozoa, and are greatly in the minority when compared with the harmless forms. The attention of investigators has been so much focussed on the disease-producing forms, on account of their practical importance, that they appear at first to overshadow the harmless forms which obtrude themselves less on the public attention, though far more numerous. Thus, if trypanosomes are mentioned, most people think at once of the deadly parasites of sleeping sickness or other diseases; and it comes almost as a shock to find that the fishes and frogs of our waters, and the wild birds and animals of this and other countries, are commonly infested with trypanosomes without being perceptibly the worse for these parasites. In fact, the disease-producing Protozoa are to be considered as exceptional and aberrant forms; the effects they produce on their hosts are detrimental to their own interests, and they are instances of what has been termed by Metchnikoff

a "disharmony" in nature. How is the existence of these lethal forms to be explained, and what is their significance? The best manner for a naturalist to attack this problem is to consider groups in which both harmful and harmless forms occur and are represented by closely allied species. Good instances of such cases are presented by the trypanosomes of mammals, of which two groups may be briefly described and discussed.

In rodents we find a group of trypanosomes of which *Trypanosoma lewisi* may be taken as a type, and I shall therefore refer to them for short as the *lewisi*-group. *Trypanosoma lewisi* flourishes in the two common species of rats (*Mus decumanus* and *M. rattus*), but not in any other animal, not even in the mouse, which has its own peculiar species of trypanosome (*T. duttoni*). Similarly *T. cuniculi* is specific to the rabbit, and *T. rabinowitschi* to the hamster. All these four trypanosomes of rodents are, however, very similar in their appearance and morphological characters, and can scarcely be distinguished except by the physiological action and reaction between them and their hosts; there can be no doubt that they are closely allied species, differing only in that each is adapted constitutionally to parasitism upon a special host. These specific trypanosomes of rodents of the *lewisi*-group are further quite harmless, under ordinary circumstances, to their hosts. When a rat becomes infected with *T. lewisi*, the trypanosomes at first multiply rapidly and swarm in the blood; then all multiplication ceases and the parasites gradually die out, after which the rat is immune to the parasite, and cannot be infected with it a second time.

Constrasting with the *lewisi*-group is another which we may term the *brucii*-group, the members of which are remarkable for their deadly powers, each species being the cause of some fatal disease. Such are *T. brucii*, the cause of nagana, or tsetse-fly disease in horses, cattle and dogs; *T. gambiense*, the cause of sleeping sickness in man; *T. evansi*, the cause of surra in horses; *T. equiperdum*, the cause of dourine in horses; and several other species. In this group also the parasites are practically indistinguishable from one another by appearance or structure; the species can only be identified by their reactions, but this is much

more difficult in the *brucii*-group, since, unlike the *lewisi*-group, the species are not limited to one particular type of host. Every member of the *brucii*-group can flourish in a great many different hosts, though there are limits even to their powers of adaptability. Thus *T. brucii* can flourish in ruminants, dogs, rats, and many other mammals, but apparently not in man. *T. gambiense* can infect man, monkeys, dogs, rats, etc., but not ruminants. When a rat is infected by *T. brucii*, the infection runs a course quite different from that of *T. lewisi*. The parasites in the former case multiply indefinitely until the blood contains more trypanosomes than blood-corpuscles, and the multiplication of the parasite is only ended by the death of the host and with it of the parasites.

Comparing and contrasting these two groups of trypanosomes, it is impossible to avoid in the first place the conviction that in each group the species are closely allied, and descended from a common ancestor. The ancestor of the *lewisi*-group had certain structural characters distinguishing it from that of the *brucii*-group, but each of these two ancestral species has given rise to a number of species which are practically indistinguishable by structural characters, and can only be differentiated by their physiological reactions. We have here a beautiful instance of species in the act of arising, and caught, so to speak, at a stage in which divergent physiological adaptation has not yet brought about structural differentiation. It is seen further that the species of the *lewisi*-group are quite specific in their reactions, and are each limited to certain definite hosts, while those of the *brucii*-group are far less specific, and are limited only to a comparatively wide range of hosts. We may reasonably regard the *lewisi*-group as the further advanced in the evolution of specific characters, and the *brucii*-group as being in a more incipient stage of specific differentiation. Finally, it is to be noted that the *lewisi*-group are typical harmless parasites, while the *brucii*-group are characteristically of the lethal type.

Further light is thrown on this question by a very interesting discovery made by Bruce with regard to *T. brucii*. He found that in districts where tsetse-fly disease was rife, *T. brucii* was to be found as a natural parasite of wild game, to which it is

apparently as harmless as *T. lewisi* to rats. By the agency of tsetse-flies, *T. brucii* is taken up from its natural hosts, and inoculated into domesticated animals of various kinds, in which it flourishes, and to which it is extremely fatal. To the native races of domestic animals it is less deadly, but imported animals, new to the country, succumb rapidly. Thus the wild game acts as a "reservoir," from which the infection of *T. brucii* spreads to other animals.

From these facts it is seen that *T. brucii* is most harmless to those hosts in which it is a "natural" parasite, that is to say, in which there is what may be termed a racial adaptation of the host to the parasites, and which are constitutionally able to withstand the disease-producing powers of the parasite. On the other hand, it is most deadly to those races in which it is a new parasite, and which possess no constitutional power of defence. The state of affairs is perfectly comparable to that seen in such a disease as measles, which is a comparatively harmless disease in Europeans, but an extremely deadly disease amongst races in which it is freshly introduced. What is the precise nature of the mechanism of attack and defence is the fundamental problem of the researches on immunity which are now being conducted with such ardour and industry by pathologists all over the world, and which cannot be discussed now. The facts of parasitism indicate clearly, however, that when a race of hosts has been long associated with a race of parasites, the hosts gradually acquire constitutional powers of resistance to the parasite, which the hosts do not possess when first brought into relations with the parasite. Hence it may be said that a new parasite will generally be a dangerous one, though it does not necessarily follow that the converse is true, and that a dangerous parasite is always a new one.

Here it must be pointed out that there are two ways in which a given species of parasite is "new" to a species of host. On general grounds we must suppose that a parasitic organism of any kind is descended from ancestors which were not parasitic. Hence there must have been a period in the evolution of any parasite when its ancestors were first adapting themselves to

parasitic life and establishing themselves in the body of their host, overcoming all resistance to their invasion. This kind of newness was probably not accompanied with lethal powers on the part of the parasite, since the capacity for reciprocal attack and defence on the part of the two organisms concerned was probably developed gradually in each organism and would tend to balance each other. The newness which is dangerous is seen where an organism with fully developed powers of parasitism in one "tolerant" host acquires the capacity for living in another host not adapted to it. This consideration throws perhaps some light on the disease-producing powers of trypanosomes in general. From the known facts of the development of trypanosomes, it seems highly probable that they have in all cases two hosts, a vertebrate and an invertebrate. There are further many considerations which indicate that they were originally parasites of the digestive tract of the invertebrate host, and that when the latter took to blood-sucking habits, the trypanosomes became accustomed to nourishing themselves on blood, and were finally able to establish themselves in the vertebrate host. This view may explain why these flagellates are always perfectly harmless to the invertebrates, their "old" hosts, and only pathogenic to vertebrates, their "new" hosts.

Returning now to the consideration of the examples specially selected, it is seen that the harmlessness of the *lewisi*-group is due to the fact that the species are specifically adapted to certain hosts and cannot maintain themselves in any other but those particular hosts. On the other hand, the lethal powers of the *brucii*-group are associated with the fact that its members, even when specifically adapted to a "natural" host, can nevertheless establish themselves also in a wide range of "new" hosts, with fatal results to the latter. If I am right in regarding the *lewisi*-group as further advanced in specific differentiation than the *brucii*-group, it then becomes probable that the natural tendency of evolution is to bring about a balance in the profit and loss account of parasite and host, and that the species of pathogenic trypanosomes of the *brucii*-group would tend in the future to become harmless parasites of certain hosts. This evolution, how-

ever, would be a long and gradual one, perhaps attained only by a painful process of natural selection of the hosts.

On the other hand, if I am right in regarding the members of the *brucii*-group as newly-arisen species descended from a common ancestral species of trypanosome, it follows that the ancestor must, through some process of variation, have developed the power of establishing itself in new hosts and invading, so to speak, fresh pastures. It may be supposed, therefore, that if this has happened once it may happen again, and that a parasite which is now specific to a single tolerant host may, by some unexplained process of variation, acquire at any time the power of infecting other hosts and so giving rise to new species of parasites ultimately. The facts of variation are at once the most patent and obvious characteristic of living beings, and the most difficult to trace to their causes; their study is of the utmost importance for understanding the evolution and the origin of species, and the phenomena of parasitism offer a field for the study of variation of a peculiar kind, that is to say, variation in physiological and constitutional rather than morphological characters. The variations in the powers of parasitic organisms are clearly of the greatest practical as well as theoretical importance, when it is seen that the spread of a parasite into new hosts is likely to be accompanied with the most deadly results to the hosts invaded by it. In fact, the origin of species amongst parasites is bound up with the question of the origin of disease. Ray Lankester has suggested* that the extinction of animals seen in past geological periods may have been in many cases due to their extirpation by some species of parasite new to them.

Thus it is seen that in the origin of species amongst parasites there are, as in other organisms, two steps: first the appearance of variations, with the resultant disharmony seen in the lethal forms; secondly, by a gradual process of reciprocal adaptation between host and parasite, the establishment of more normal harmonic relations, associated with definite specific characteristics and reactions on the part of the parasite and host.

* *Quarterly Review*, No. 399 (July, 1904), p. 134.

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